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Catheter-retaining Balloon-occluded Retrograde Transvenous Obliteration for Gastric Varices

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Abstract

Purpose: We evaluated the effectiveness of catheter-retaining balloon-occluded retrograde transvenous obliteration (BRTO).

Patients and Methods: Patients were divided into 2 groups based on concurrent contrast imaging findings. The primary endpoint was effectiveness, the secondary endpoint was complications, and the tertiary endpoint was recurrence of esophageal varices in all cases.

Results: The mean volume of EO administered was 16.43±4.37 overall and was significantly lower in group 1 (40.61±14.95 mL; 15 patients, 32.6%) than in group 2 (31 patients, 67.4%). The number of injections was 1.60±0.63 in group 1 and 2.97±0.60 in group 2, and the volume of EO used in 1 day did not differ significantly between group 1 (12.28±6.48 mL) and group 2 (13.54±3.12 mL). The disappearance rate of varices was significantly greater in group 1 (100%) than in group 2 (90.3%). Fever developed in 33.3% of patients in group 1 and 87.1% of patients in group 2. The rates of recurrence of esophageal varices 2, 4, and 9 years after the procedure were 34%, 48%, and 57%, respectively.

Conclusion: These results show that catheter-retaining BRTO is a simple and highly effective procedure for difficult cases with minor complications. Furthermore, catheter-retaining BRTO does not require a large daily dose of EO and is, therefore, an effective treatment for solitary gastric varices.

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Key words: balloon-occluded retrograde transvenous obliteration, catheter-retaining balloon-occluded retrograde transvenous obliteration, gastric varices, ethanolamine oleate

Introduction

In 1984, Olson et al.[1] successfully treated gastric varices by embolizing the gastrorenal shunt with ethanol. However, this technique did not become widespread presumably because of ethanol-related damage to blood vessels and its limited effect on gastric varices. Later, in 1996, Kanagawa et al.[2] performed a similar technique using 5% ethanolamine oleate (EO). Although 5% EO as a sclerosing agent for esophageal varices was shown to be safe and effective, it did not gain wide acceptance, perhaps because it did not remain in gastric varices. In the same year, Chikamori et al.[3] reported an approach through the internal jugular

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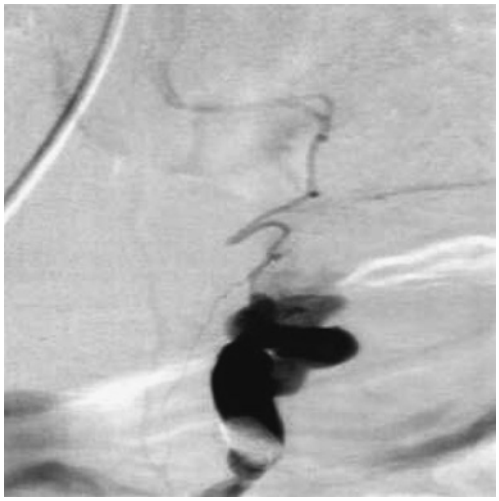

Fig. 1 First day of BRTO. EO (20 mL) was injected and only a part of the shunt vessel opacifies because of the large vessel size.

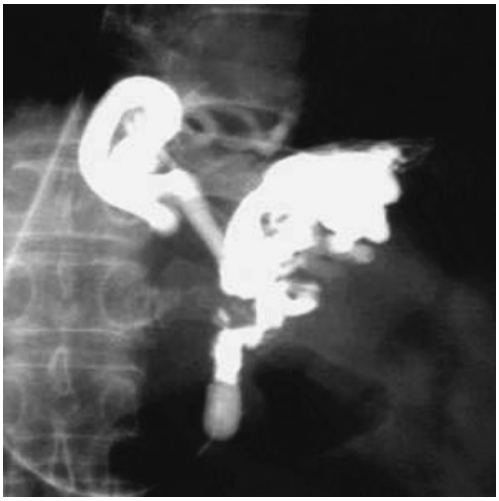

Fig. 2 Second day of BRTO. All of the gastric varices and feeding vein (left gastric vein) are contrasted. Here, catheter-retaining BRTO is complete.

vein, while our group[4] reported the use of an indwelling catheter. Both methods proved to be effective and spread rapidly across Japan.

Here we investigated the safety and effectiveness of catheter-retaining balloon-occluded retrograde transvenous obliteration (BRTO) for many additional cases.

Patients and Methods

Catheter-retaining BRTO

A balloon catheter (TMC-KAKUTANI, 7-Fr; Clinical Supply, Inc., Tokyo, Japan) was inserted into a gastrorenal shunt via the right internal jugular vein and placed as close as possible to gastric varices. Shunt venography was performed after the blood flow was blocked with the balloon, and 20 mL or less of the sclerosant, 5% EO, was administered **(Fig. 1)**. The 5% EO was prepared by combining equal volumes of 10% EO and the contrast agent. In the present study, we set the maximum daily dose of EO at 20 mL which is the maximum dose allowed by Japanese Ministry of Health, Labour and Welfare.

The EO was injected, and the catheter was retained until the following day. If imaging performed on the following day failed to show complete embolization of all gastric varices, additional EO was injected until complete embolization was achieved **(Fig. 2)**. When complete embolization was confirmed, the balloon was removed. No haptoglobin was used.

Patients

The patients had solitary gastric varices and met the following criteria:

1) F2 or F3 gastric varices with a moderate to severe red color sign, according to the general rules for recording endoscopic findings of esophagogastric varices[5].

2) F2 varices were moderately enlarged and beady, and F3 varices were markedly enlarged, nodular or tumor-shaped varices. The red color sign indicates that changes of a reddish color were seen immediately beneath the submucosa.

3) No previous treatment for gastric varices

4) No portal thrombosis or arterioportal shunt on arterioportography or contrast-enhanced computed tomography

5) Mild or no esophageal varices

Exclusion criteria were as follows: 1) total bilirubin ≥3 mg／dL, 2) Child-Pugh score ≥12, 3) encephalopathy, 4) intractable ascites; 5) previous laparotomy, and 6) coexisting ectopic varices.

The subjects were 31 men and 15 women with a mean age of 59 years. The Child-Pugh score was A in 22 patients, B in 13 patients, and C in 11 patients. Fifteen patients had both hepatic cirrhosis and

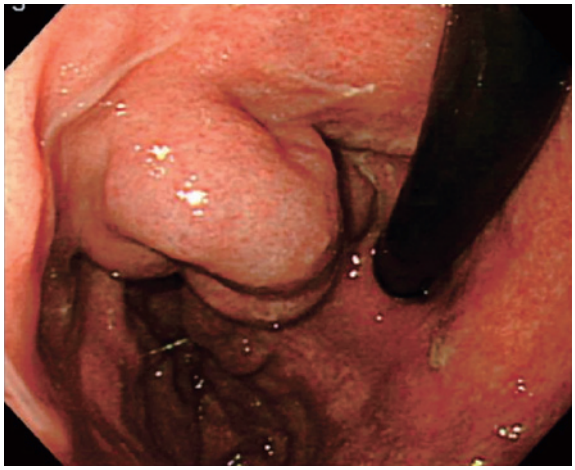

Fig. 3 Endoscopic findings before BRTO show large gastric varices.

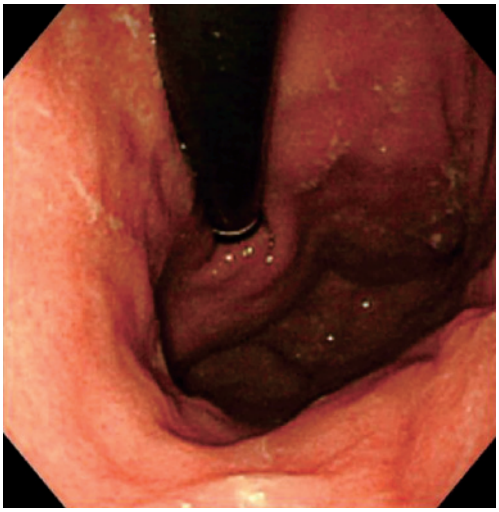

Fig. 4 Gastric varices have disappeared 2 months after BRTO.

hepatocellular carcinoma, and 31 patients had hepatic cirrhosis alone. The BRTO procedures were emergent in 1 case, elective in 11 cases, and prophylactic in 34 cases.

Methods

Forty-six patients were enrolled and divided into 2 groups. Group 1 consisted of patients in whom 20 mL or less of 5% EO was given to visualize gastric varices and the feeder vein, such as the left gastric vein and posterior gastric vein. Group 2 consisted of patients in whom all of the gastric varices could not be visualized after administration of 20 mL of contrast agent because of a large gastrorenal shunt or another systemic shunt.

Group 1 was considered an easy-to-treat group, and group 2 was considered a difficult-to-treat group. In this study, we examined whether catheter-retaining BRTO is a useful and safe treatment for gastric varices, including difficult-to-treat cases.

The primary endpoint was effectiveness, the secondary endpoint was complications, and the tertiary endpoint was recurrence of esophageal varices in all cases.

Gastric varices were evaluated with endoscopy monthly after BRTO **(Fig. 3, 4)**.

Esophageal varices was check by endoscopy every 4 months.

The study protocol was approved by the institutional ethics committee, and written informed consent was obtained from each patient before the procedure.

Results

Group 1 included 15 patients (32.6%), and group 2 included 31 patients (67.4%).

The mean total volume of EO used was 32.73±16.92 mL overall and was significantly greater in group 2 (40.61±14.95 mL) than in group 1 (16.43±4.37 mL) **(Fig. 5)**. The mean number of times EO was injected was 2.52±0.89 overall and was significantly greater in group 2 (2.97±0.60) than in group 1 (1.60±0.63). The mean volume of EO injected in 1 day was 13.13±4.46 mL overall and did not differ significantly between group 1 (12.28±6.48 mL) and group 2 (13.54±3.12 mL).

The disappearance rate of gastric varices was 100% in group 1 and 90.32% in group 2 **(Fig. 6)**.

Although fever developed in 33.3% of patients in group 1 and 87.1% of patient in group 2, no serious complications, such as pulmonary infarction and renal failure, occurred, and gastric varices did not recur. However, 1 patient had bleeding from esophageal varices. The rates of recurrence of esophageal varices 2, 4, and 9 years after the procedure were 34%, 48%, and 57%, respectively **(Fig. 7)**.

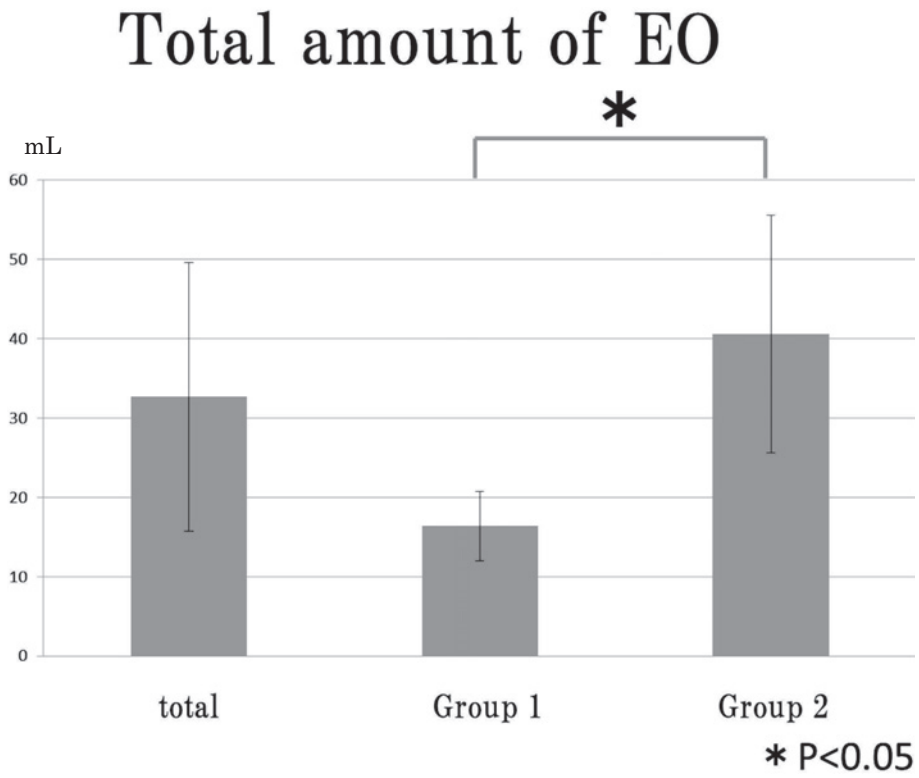

Fig. 5 The total volume of EO was significantly greater in group 2 than group 1
EO: Ethanolamine oleate

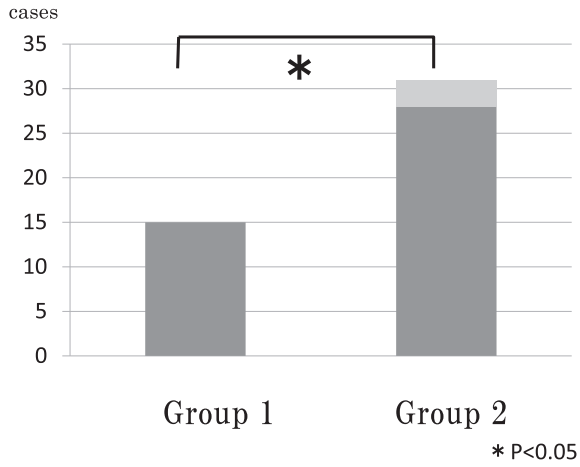

Fig. 6 Disappearance rate of gastric varices
The disappearance rate of gastric varices was significantly higher in group 1 than group 2.

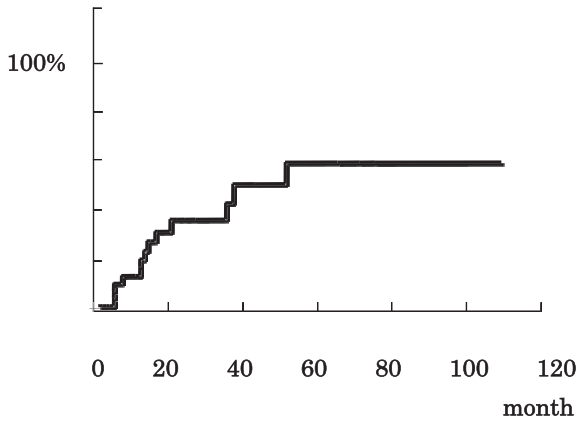

Fig. 7 The recurrence rate of esophageal varices

Discussion

The frequency of gastric variceal bleeding is generally less than that of esophageal variceal bleeding; however, gastric variceal bleeding may be fatal[6–9]. A number of surgical procedures have been replaced by minimally invasive endoscopic therapy and the use of the transjugular intrahepatic portosystemic shunt for the treatment of gastric varices. However, because of large vessel sizes and high blood flow, the use of endoscopy to treat gastric varices is difficult. Even though hemostasis can be achieved with the use of cyanoacrylate, complete obliteration of gastric varices in endoscopic therapy remains challenging and is associated with high rates of recurrence, recurrent bleeding, and in-

hospital mortality[10–12]. Although Kind et al. have reported a high hemostasis rate of 97.1% using cyanoacrylate, they have also reported an early recurrent bleeding rate of 15.5% and an in-hospital mortality rate of 19.5%[11]. In addition, Ramond et al. performed endoscopic therapy with cyanoacrylate in 27 patients: of these patients 10 had recurrent bleeding and 8 died[12]. Moreover, the amount of bleeding is large when cyanoacrylate is used in an attempt to achieve hemostasis; even if hemostasis is achieved, endoscopic therapy is associated with a mortality rate of 25% to 55% due to liver failure[6–9].

BRTO was performed in 1996 by Kanagawa et al. in Japan when no definitive treatment for gastric varices was available[2]. This method was first reported by Olson et al. in 1984[1] but did not become popular, presumably because of its limited efficacy and the adverse effects of ethanol. Kanagawa et al. used, instead of ethanol, 5% EO, which had already been used successfully in the embolization of esophageal varices. In 1996, Chikamori et al. reported an approach through the jugular vein[3] which has the advantage of allowing a catheter to be inserted deeply into a shunt. Similarly, they used ethanol to obliterate the other blood-draining routes of varices. In the same year, we reported catheter-retaining BRTO, in which a catheter is left in place until the following day to enable re-injection of the agent, if necessary[4].

The advantage of our technique is that the daily dose of EO can be maintained in a safe range owing to the fractionated nature of the treatment. In addition, unforeseen events, such as damage to the balloon, can be handled safely. Such techniques were used mainly for prevention any complication in Japan. Endoscopists and internal medicine specialists, who had been experiencing difficulties in treating gastric varices, became the leading forces behind prophylactic treatment.

In 1997, Kim et al. revealed the natural history of gastric varices, with 1-, 3-, and 5-year bleeding rates of 16%, 36%, and 44%, respectively[9]. Risk factors were observed to be large size and the red color sign. With this report as the theoretical background, the number of prophylactic treatments for large gastric varices and varices with the red color sign has increased markedly.

The overall disappearance rate of gastric varices in the present study was 93.5%. This rate was similar to those in other studies, which used 50% glucose and microcoils[13,14] and suggests the simplicity and safety of catheter-retaining BRTO. Moreover, as has been reported as a characteristic of BRTO[15–17], no recurrence of hemorrhage was seen when BRTO was successful.

A serious challenge associated with BRTO is finding a way to reduce the volume of the sclerosing agent EO. When a large amount of EO is necessary to embolize gastric varices, balloon damage can immediately lead to serious complications or death.

Our method is safe because the maximum daily volume of 20 mL cannot be exceeded. Even if all gastric varices cannot be embolized in 1 day, the remaining varices can be embolized on the following day. Thus, our method is a fractionated embolization method.

In the present study, patients in whom all gastric varices could be visualized more than 20 mL EO accounted for approximately 30% of subjects (group 1), and the remaining 70% of patients required less than 20 mL EO (group 2). Patients in group 2 were considered difficult to treat because of a large gastrorenal shunt or another systemic shunt.

The total volume of the sclerosing agent was 32.73±16.92 mL overall and was greater in group 2 (40.61±14.95 mL) than in group 1 (16.43±4.37 mL); however, the volume of EO per day was approximately 13 mL in both groups and did not differ significantly between the groups. This volume also shows that we completed the treatment with half the amount of sclerosant used by Kanagawa et al.[2] (mean volume, 27.7 mL). The amounts of EO used in other studies were 30±2.1 mL[18], 27.6±12.8 mL[19], 18.75 mL[20], 25.7±19.1 mL[17], and 18.5±5.5 mL[21] and demonstrate the safety of catheter-retaining BRTO.

Although we did not use haptoglobin in this study, the frequency of hematuria was approximately 60%, which is not significantly different from the frequencies in studies in which haptoglobin used[19,22,23]. However, indwelling catheterization was associated with a higher incidence of fever, and further study is needed to determine whether the development of

fever can be attributed to indwelling catheterization.

This study had several limitations. We failed to compare the present technique with other new methods. The catheter is retained in our BRTO procedure, and the shunt vessel is not completely embolized the following day; however, the volume of sclerosing agent can be reduced more effectively if the agent is injected as close as possible to the gastric varice. Recently, many attempts have been made to reduce the volume of sclerosing agent used, by, for example, the use of microcatheters[24,25], 50% glucose, embolization coils[26], and foam BRTO[27,28]. Further studies are needed to compare the present technique with these other new methods in the future.

It is also necessary to be aware of the risk associated with long-term retention of the balloon catheter. Because thrombus has been reported to occur after a balloon catheter is retained in a vein for several days[29], more detailed studies are needed.

Exacerbation of esophageal varices can be considered a long-term complication of BRTO. After a long observation period, esophageal varices worsened in approximately half the patients who underwent BRTO. This high rate of worsening is because BRTO is performed to embolize shunt vessels and inevitably leads to the development of other collateral circulation. We plan to investigate if shunt vessels should be left intact, if possible.

Conclusion

It was possible to perform catheter-retaining BRTO with low daily doses of EO. With this method, we successfully treated difficult cases with large vascular volumes and multiple blood drainage pathways without causing serious complications. Indwelling catheters are retained in place to deliver a prefractioned sclerosing agent, and thus catheter-retaining BRTO is a simple, safe, and highly successful method worth exploring.

Conflict of Interest: No authors have financial relationships relevant to this publication to disclose.

References

1. Olson E, Yune HY, Klatte EC: Transrenal-vein reflux ethanol sclerosis of gastroesophageal varices. AJR Am J Roentgenol 1984; 143: 627–628.
2. Kanagawa H, Mima S, Kouyama H, Gotoh K, Uchida T, Okuda K: Treatment of gastric fundal varices by balloon-occluded retrograde transvenous obliteration. J Gastroenterol Hepatol 1996; 11: 51–58.
3. Chikamori F, Shibuya S, Takase Y, Ozaki A, Fukao K: Transjugular retrograde obliteration for gastric varices. Abdom Imaging 1996; 21: 299–303.
4. Kakutani H, Sanada J, Tsukioka Y, et al.: Transvenous obliteration of portosystemic shunt (TOPS) for control of solitary gastric varices. Endoscopy 1996; 28: S14.
5. Tajiri T, Yoshida H, Obara K, et al.: General Rules for Recording Endoscopic Findings of Esophagogastric Varices (The 2nd Edition). Digestive Endosc 2010; 22: 1–9.
6. Trudeau W, Prindiville T: Endoscopic injection sclerosis in bleeding gastric varices. Gastrointest Endosc 1986; 32: 264–268.
7. Sarin SK, Sachdev G, Nanda R, Misra SP, Broor SL: Endoscopic sclerotherapy in the treatment of gastric varices. Br J Surg 1988; 75: 747–750.
8. Sarin SK, Lahoti D, Saxena SP, Murthy NS, Makwana UK: Prevalence, classification and natural history of gastric varices: a long-term follow-up study in 568 portal hypertension patients. Hepatology 1992; 16: 1343–1349.
9. Kim T, Shijo H, Kokawa H, et al.: Risk factors for hemorrhage from gastric fundal varices. Hepatology 1997; 25: 307–312.
10. Schubert TT, Schnell GA, Walden JM: Bleeding from varices in the gastric fundus complicating sclerotherapy. Gastrointest Endosc 1989; 35: 268–269.
11. Kind R, Guglielmi A, Rodella L, et al.: Bucrylate treatment of bleeding gastric varices: 12 years' experience. Endoscopy 2000; 32: 512–519.
12. Ramond MJ, Valla D, Mosnier JF, et al.: Successful endoscopic obturation of gastric varices with butyl cyanoacrylate. Hepatology 1989; 10: 488–493.
13. Ninoi T, Nishida N, Kaminou T, et al.: Balloon-Occluded Retrograde Transvenous Obliteration of Gastric Varices with Gastrorenal Shunt: Long-Term Follow-Up in 78 Patients. AJR 2005; 184: 1340–1346.
14. Akahoshi T, Hashizume M, Tomikawa M, et al.: Long-term results of balloon-occluded retrograde transvenous obliteration for gastric variceal bleeding and risky gastric varices: A 10-year experience. Journal of Gastroenterology and Hepatology 2008; 23: 1702–1709.
15. Hirota S, Matsumoto S, Tomita M, Sako M, Kono M: Retrograde transvenous obliteration of gastric varices. Radiology 1999; 211: 349–356.
16. Matsumoto A, Hamamoto N, Nomura T, et al.: Balloon-occluded retrograde transvenous obliteration of high-risk gastric fundal varices. Am J Gastroenterol 1999; 94: 643–649.
17. Kitamoto M, Imamura M, Kamada K, et al.: Balloon-occluded retrograde transvenous obliteration of gastric fundal varices with hemorrhage. AJR 2002;

178: 1167–1174.
18. Yamagami T, Kato T, Hirota T, Yoshimatsu R, Matsumoto T, Nishimura T: Infusion of 50% glucose solution before injection of ethanolamine oleate during balloon-occluded retrograde transvenous obliteration. Australasian Radiology 2007; 51: 334–338.
19. Shimoda R, Horiuchi K, Hagiwara S, et al.: Short-term complications of retrograde transvenous obliteration of gastric varices in patients with portal hypertension: effects of obliteration of major portosystemic shunts. Abdom Imaging 2005; 30: 306–313.
20. Tanoue S, Kiyosue H, Matsumoto S, et al.: Development of a new coaxial balloon catheter system for balloon-occluded retrograde transvenous obliteration (B-RTO). Cardiovasc Intervent Radiol 2006; 29: 991–996.
21. Sugimori K, Morimoto M, Shirato K, et al.: Retrograde transvenous obliteration of gastric varices associated with large collateral veins or a large gastrorenal shunt. J Vasc Interv Radiol 2005; 16: 113–118.
22. Koito K, Namieno T, Nagakawa T, Morita K: Balloon-occluded retrograde transvenous obliteration for gastric varices with gastrorenal or gastrocaval collaterals. AJR 1996; 167: 1317–1320.
23. Sonomura T, Sato M, Kishi K, et al.: Balloon-occluded retrograde transvenous obliteration for gastric varices: a feasibility study. Cardiovasc Intervent Radiol 1998; 21: 27–30.
24. Sonomura T, Ono W, Sato M, et al.: Three benefits of microcatheters for retrograde transvenous obliteration of gastric varices. World J Gastroenterol 2012; 28: 1373–1378.
25. Minamiguchi H, Kawai N, Sato M, et al.: Dual Microcatheter Retrograde Transvenous Obliteration of Gastric Varices: Coil Embolization as a Substitute for Balloon Occlusion. Case Rep Gastroenterol 2012; 6: 74–81.
26. Yamagami T, Tanaka O, Yoshimatsu R, Miura H, Nishimura T: Value of embolisation of collateral veins from gastric varices before balloon-occluded retrograde transvenous obliteration. Journal of Medical Imaging and Radiation Oncology 2011; 55: 26–32.
27. Koizumi J, Hashimoto T, Myojin K, et al.: Balloon-Occluded Retrograde Transvenous Obliteration of Gastric Varices: Use of CT-Guided Foam Sclerotherapy to Optimize Technique. AJR 2012; 199: 200–207.
28. Choi SY, Won JY, Kim KA, et al.: Foam sclerotherapy using polidocanol for balloon-occluded retrograde transvenous obliteration (BRTO). Eur Radiol 2011; 21: 122–129.
29. Yoshimatsu R, Yamagami T, Tanaka O, et al.: Development of Thrombus in a Systemic Vein after Balloon-Occluded Retrograde Transvenous Obliteration of Gastric Varices. Korean J Radiol 2012; 13: 324–331.

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